UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,116	12/09/2005	Stefan-Lutz Wollin	27074U	2977

34375 7590 10/17/2006

NATH & ASSOCIATES PLLC
112 South West Street
Alexandria, VA 22314

EXAMINER	
KHANNA, HEMANT	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 10/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/560,116	WOLLIN, STEFAN-LUTZ	
	Examiner	Art Unit	
	Hemant Khanna	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-25 and 29-48* is/are pending in the application.

4a) Of the above claim(s) *6,13,16-25,29-33 and 36-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-5,7-12,15,34 and 35* is/are rejected.

7)☒ Claim(s) *14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/23/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of claims 3-5, 7-12, 14-15, and 34-35 that belong to Group I in the reply filed on September 15, 2006 is acknowledged.

Applicant's elected the species corresponding to the pulmonary surfactant of lusupultide and a PDE5 inhibitor of sildenafil. Because the Applicant has not identified the claims that are readable on the elected species, the Examiner submits that the non-election of claims readable on the species is non-responsive. However, in the interest of facilitating prosecution, the Examiner has determined which claims embraced by the elected species are under examination. Applicant's species of lusupultide reads on claims 3-5, 7-8, 15 and 35. Applicant's species of sildenafil reads on claims 3-5, 9-12, 15, and 34-35. Therefore, claims 3-5, 7-12, 15, and 34-35 have been examined on the merits.

Applicant's species have not been found free of the prior art and the claims that read on the species stand rejected under 35 USC 102 as set forth below.

Claims 3-5, 7-12, 15, 34-35 are pending.

Claims 6, 13, 29-33, 16-25, 36-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 15, 2006.

Claim Objections

2. Claim 14 is objected to as depending from a non-elected claim, claim 13. The Examiner had inadvertently left claim 14 in the invention of Group I when requesting for a restriction between inventions in the Action dated August 21. During examination of the case, the Examiner requested the Applicant for withdrawal of claim 14, however the withdrawal was not authorized. The examiner recommends rewriting claim 14 to depend from claim 12, however, in so doing the Examiner respectfully submits that claim 14 will be subject to the same grounds for rejection as they applied to claim 12.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 3-5, 7-12, 14-15, 34-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The specification, while being enabling for methods to evaluate the treatment by pulmonary surfactants and PDE5 inhibitors individually, does not reasonably provide enablement for the prevention of diseases that originate from pulmonary surfactant malfunction and detrimental phosphodiesterase 5 activity by the synergistic administration of pulmonary surfactants and phosphodiesterase 5 inhibitors. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

Nature of the invention. In the instant case, the claims are drawn to methods of preventing or reducing the onset of symptoms of a disease in which the pulmonary surfactant malfunction and/or phosphodiesterase 5 activity is detrimental in a patient comprising the administration of a pulmonary surfactant and a PDE5 inhibitor.

State and un/predictability of the prior art. At the time the invention was made, the successful prevention of a disease that resulted from the pulmonary surfactant

malfunction and/or phosphodiesterase 5 activity, was not routinely obtainable by those skilled in the art. It is presumed that the Applicant's intent is to prevent diseases that may result from phosphodiesterase 5 activity and not treat diseases resulting from the activity or malfunction of the pulmonary surfactant. Since the success of the former reads on effectively predicting a condition that will result before the development of a disease, the prevention is not enabled in view of the contemporary knowledge in the art. This is reflected by the findings in a published manuscript. Wilkins et al teach that as of March 2003, "Sildenafil has been used as a drug of last resort in human infants" (page 59, first paragraph). Since the treatment of ARDS with sildenafil is the last resort in human infants, one skilled in the art would conclude that the aspect of preventing ARDS by sildenafil cannot be expected in view of the knowledge in the art that suggests that treatment of such conditions by sildenafil should only be a last resort. Therefore, preempting the prevention of ARDS by sildenafil, in favor of a last resort treatment by sildenafil.

Working examples. Although examples are disclosed in the specification, no examples indicate the prevention of pulmonary diseases by the administration of both phosphodiesterase -5 inhibitors and pulmonary surfactants.

Guidance in the specification. The specification provides little guidance regarding practice of the claimed methods. The specification has provided examples of the commercial availability of the individual phosphodiesterase 5 inhibitors and pulmonary surfactants. However, the specification does not explicitly administer the above-

mentioned compounds together or successively to yield a preventative endpoint in pulmonary therapy.

Amount of experimentation necessary. Given the unpredictability of the art in view of prevention of ARDS with phosphodiesterase 5 inhibitors, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate with the scope of the claims. Although the applicants have identified an interesting synergistic use of phosphodiesterase 5 inhibitors with pulmonary surfactants which may play a role in treating pulmonary diseases, but essentially all of the work required to ultimately develop a prevention method has been left for others.

For the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 3, 9-12, 15, 34-35 rejected under 35 U.S.C. 102(b) as being anticipated by Wilkins et al (Clinical Techniques in Equine Practice (2003) Vol. 2 pages 56-66).

Claims 3, 9-12, 15, 34-35 are drawn to a method for preventing or reducing the onset of symptoms of a disease comprising the administration of the elected species of PDE5 inhibitor, namely sildenafil (5-[2-ethoxy-5-(4-methyl-1-piperazinylsulfonyl) phenyl]-

1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo [4, 3-d]pyrimidin-7-one); selected from a group of PDE5 inhibitors and a pulmonary surfactant.

Wilkins et al disclose the intravenous administration of sildenafil, which is a novel therapy investigated in human infants with specificity as a pulmonary vasodilator to remove vascular resistance in pulmonary tissue (left column, first paragraph, page 59). Wilkins et al further disclose the treatment of surfactant dysfunction, by instilling exogenous surfactants, the absence of which causes acute respiratory failure and acute respiratory distress syndrome (RDS, left column, second paragraph, page 65), thus meeting all the limitations of claims 3, 9-12, 15, 34-35.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 3-5, 7-12, 15, and 34-35 rejected under 35 U.S.C. 103(a) as being unpatentable over Wilkins (Clinical Techniques in Equine Practice (2003) Vol. 2 pages 56-66) in view of Hafner et al (WO 01/76619).

Claims 3-5, 7-12, 15, and 34-35 are drawn to a method for preventing or reducing the onset of symptoms of a disease comprising the administration of a pulmonary surfactant and a PDE5 inhibitor.

Wilkins et al disclose the intravenous administration of sildenafil (as in instant claims 9-12, 34), a phosphodiesterase-5 inhibitor (as in instant claim 3), which is a novel therapy currently being investigated in human infants with specificity as a pulmonary vasodilator to remove vascular resistance in pulmonary tissue (left column, first paragraph, page 59). In piglets the administration of sildenafil, reversed the increase in pulmonary vascular resistance within 1 hour of commencing the infusion. Wilkins et al also disclose the treatment of surfactant dysfunction, by instilling exogenous surfactants. Further, Wilkins et al disclose that the inactivation of pulmonary surfactant may be important in acute respiratory failure and acute respiratory distress syndrome (RDS, left column, second paragraph, page 65; as in instant claims 15 and 35). Wilkins et al do not disclose the co-administration of the pulmonary surfactant and a PDE5 inhibitor.

Hafner et al teach methods that use the recombinant pulmonary surfactant proteins designated as lusupultide (as in instant claims 7-8) for the treatment of pulmonary diseases (claim 6), selected from ALI, ARDS, acute respiratory insufficiency, pneumonias, nasocomial infections or SIRS (page 3, second paragraph, as in instant claims 15, 35). Hafner et al do not teach the administration of a phosphodiesterase-5 inhibitor.

It has been held that the combination of two or more compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is to be used for the very same purpose. In re Kerkhoven, 205 USPQ 1069, 1072 (CCPA 1980); In re Susi, 169 USPQ 423, 426 (1971); In re Crockett 126 USPQ 186, 188 (1960). As the court explained in Crockett, the idea of combining them flows logically from their having been individually taught in the prior art. It would have been obvious to one of ordinary skill in the art to combine the administration of sildenafil, and lusupultide. One would have been motivated to use the co-administration of both sildenafil and lusupultide in view of the teachings of both Wilkins et al and Hafner et al who suggest the individual uses of both sildenafil and lusupultide for the treatment of pulmonary diseases. There would have been a reasonable expectation of success in view of the teachings of Wilkins et al who teach therapeutic modalities of phosphodiesterase-5 inhibitors and surfactants to treat the causes of acute respiratory failure.

With regards to the simultaneous or successive administration of sildenafil and lusuptide, it would have been obvious to one skilled in the art at the time of invention to

determine the order of administration, because the orders of administration are art recognized variables that are routinely determined and optimized.

Duplicate Claims

8. Applicant is advised that should claim 9 be found allowable, claim 10 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

9. Applicant is advised that should claim 15 be found allowable, claim 35 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

10. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hemant Khanna whose telephone number is (571) 272-9045. The examiner can normally be reached on Monday through Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hemant Khanna
October 12, 2006

B. DELL CHISM
PATENT EXAMINER